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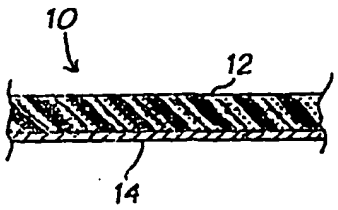
(54) Title: ANTIMICROBIAL COMPOSITION AND ARTICLES



(57) Abstract: A multilayered antimicrobial composition (10) in sheet form, articles of manufacture that include the composition, and a method for making the composition. The composition includes a layer of polymeric material (12) and a layer (14, 16) containing an antibacterial metal; in a preferred embodiment, the polymeric material (12) is a gel composition comprising a block copolymer and, optionally, mineral oil; the antibacterial layer (14, 16) is provided by coating the gel composition (12) with silver, incorporating silver into the gel composition, or attaching a silver-containing fabric to the gel composition. The composition (10) itself is durable, nontoxic, nonhazardous, substantially nonallergenic and nonirritating, and inert until activated by contact with a suitable liquid (water, perspiration, wound exudate, hydrocolloid, etc.). It may be used in a variety of products, including but not limited to wound dressings, pressure dressings, knee, wrist and elbow sleeves, heel and sole inserts, and the like.

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ANTIMICROBIAL COMPOSITION AND ARTICLES

TECHNICAL FIELD OF THE INVENTION

The present invention relates to an antimicrobial composition in the form of a generally flat, cushioned sheet. In particular, the present invention relates to a multilayer sheet composition including a polymer layer and a silver-containing layer, to articles of manufacture such as wound packing materials, dressings for the care and treatment of surface wounds, sole and heel pads, knee and elbow sleeves, socks, wraps and compression wraps, and the like made with the composition, and to a method for making the composition.

BACKGROUND ART

The care and treatment of wounds is an important part of health care, incorporating the sometimes-irreconcilable goals of satisfactory outcomes, responsiveness to patient concerns, and cost-effectiveness. Wound healing is a cellular process which is triggered by the occurrence of an injury (as used herein, the terms "wound" and "injury" refer to tissue damage or loss of any kind, including but not limited to cuts, incisions (including surgical incisions), abrasions, lacerations, fractures, contusions, burns, amputations, and so forth). Healing is believed to be controlled by a biophysiological feedback mechanism that monitors the extent of the injury and controls cellular activity in the injured area to produce the types and numbers of cells needed to accomplish a repair.

Many conditions can impact normal healing processes, including impaired circulation, conditions such as diabetes and infections at the situs of the injury which frequently result in non-healing or slowly-healing wounds, unfavorable outcomes, and increased health care costs. In response to these concerns, many hospitals have established specialized centers to treat non-healing wounds. A wide variety of treatment modalities, including local and systemic antibiotics, antibiotic-impregnated dressings, antibiotic and antifungal compositions, and the like are available for treating infected wounds, slowly-healing wounds, and non-healing wounds. Many of these are used prophylactically in an attempt to forestall infections, which are a growing concern due to the spread of antibiotic-resistant strains of bacteria.

Many different materials are used for manufacturing wound dressings, surgical gowns and masks, surgical drapes, and like products. Available materials may include flexible, conformable substrates, moisture-absorbing layers, gas-permeable and liquid-impermeable layers, selectively-permeable layers, non-adhering or self-adhering layers, and moisture-absorbing layers, of natural fibers or man-made compositions. Antibacterial agents may be added for therapeutic purposes or to increase the shelf life of the product.

By way of example, Kania (U.S. No. 5,603,122, incorporated herein by reference) describes a form-fitting sleeve member that incorporates a polymeric cushioning material (most preferably a thermoplastic elastomer, silicon-containing elastomer, or thermoset silicone). The cushioning material may include additives such as antioxidants, skin conditioning agents, astringents, biocides, and other medicaments. Delmore, et al. (U.S. No. 5,939,339) discloses a bandage having a porous, self-adhering elastic substrate which does not adhere to clothing, hair or skin, and which has a permanent compressive force that is sufficient to hold it in place. Caldwell, et al. (U.S. No. 5,856,245) describe a polymer composition that is impermeable to liquids, permeable to gases, and impermeable (or selectively permeable) to microorganisms. The fabric can be attached to a layer of absorbent polymer, and can incorporate a wide range of additives including growth factor, wound healing proteins such as collagen, electromagnetic and electrostatic shielding agents, electrically conducting agents, and a variety of antimicrobial agents.

Additional materials are described by Strack, et al. (U.S. No. 5,681,545), Moretz, et al. (U.S. Nos. 5,217,782; 5,210,882; 5,297,296), Hagiwara, et al. (U.S. No. 4,525,410), Seymour (U.S. Nos. 4,460,369 and 4,340,043). Wound dressings are disclosed by Widemire (U.S. 5,782,788), Lang, et al. (U.S. Nos. 4,860,737 and 4,753,231), Matson (U.S. No. 4,728,323), Rawlings, et al. (U.S. No. 4,657,006), Augurt (U.S. No. 3,903,882), McKnight, et al. (U.S. No. 3,800,792), Maeth, et al. (U.S. No. 3,249,109), and Stowasser, et al. (U.S. No. 2,934,066). Sims (U.S. No. 4,638,796) provides a method for dressing a wound with a nonadherent, nonabsorbent, conformable material, followed by an absorbent dressing. An antimicrobial agent may be applied to the material.

Wound dressings and other products may include antimicrobial additives to retard spoilage and increase shelf life. See, for example, Erami (U.S. No. 5,478,563), Hagiwara, et al. (U.S. No. 5,413,789), Niira, et al. (U.S. Nos. U.S. Nos. 4,938,958 and 4,938,955), and Barth, et al. (U.S. No. 4,376,763). Some products contain leachable antimicrobial compositions, for example, Capelli (U.S. Nos. 5,326,567 and 4,933,178), Jacobson, et al. (U.S. No. 5,180,585), Yazaki, et al. (U.S. No. 5,094,847), Edwards, et al. (U.S. No. 4,906,466), Leibovich, et al. (U.S. No. 4,808,402), Laurin, et al. (U.S. No. 4,603,152), and Romans (U.S. No. 3,092,552).

Silver and other metals have been widely used in antimicrobial and antifungal applications, including topical preparations (creams, ointments, etc.) as well as wound dressings. (For purposes of this detailed description, a metal with "antibiotic," "antimicrobial," "cidal," "bactericidal" and/or "bacteristatic" properties is broadly defined as a metal that is active against at least one pathogenic microorganism, including but not limited to bacteria, protozoa, fungi, rickettsiae, and viruses. Bactericidal agents kill microorganisms, whereas bacteristatic agents prevent their growth and multiplication.) Silver has good bioactivity at relatively low concentrations, thus, it is perhaps the most widely-used antimicrobial metal. Topical preparations that contain silver or silver compounds—silver

nitrate, silver sulfadiazine, colloidal silver compositions, silver-protein compounds such as Argyrol™, and so forth—are widely used in medicine. For example, ointments containing silver sulfadiazine are widely used for the treatment of infected burns.

The introduction of antibiotics in the 1940s revolutionized the treatment of systemic bacterial infections such as pneumonia and septicemia. However, the direct use of antibiotics in localized, infected wounds proved to be unsatisfactory due to their irritative and allergic effects on human tissues. As a result, such infections are frequently treated with systemic administration of antibiotics. Now, however, the nature of infectious processes has been greatly changed with the spread of antibiotic-resistant strains, the prevalence of mixed infections, and the dearth of new antibiotics. As a result, the effective treatment of local infections has become much more difficult, requiring systemic administration of large doses of multiple antibiotics often with attendant undesirable side effects.

Even after the introduction of antibiotics, infections of bone (i.e., osteomyelitis) remained difficult to treat because the limited blood supply to this tissue precluded obtaining adequate local levels of systemically administered antibiotics. The appearance of mixed and antibiotic-resistant infections has further complicated this situation. Even today, the only effective treatment for osteomyelitis remains primarily surgical, and includes adequate wound débridement, leaving the wound open during healing, and supplementing with appropriate systemic antibiotics.

The effectiveness of silver as an antimicrobial agent is at least partly determined by the delivery system. Most silver compounds that dissociate readily yield cations that are highly toxic to human tissues, and therefore are not considered suitable for medical use. Less-toxic compounds, including silver sulfadiazine cream (widely used in the treatment of burns) and silver nitrate solution, do not dissociate readily. These topical compounds must therefore be re-applied frequently to maintain their clinical efficacy.

Iontophoretic (i.e., electrically-generated) silver ions, which can penetrate more deeply into the tissues than silver ions from topical compounds, have been found to inhibit bacterial and fungal growth in vivo and in vitro at current densities as low as 10 nA/mm^2. Silver ions are effective even against antibiotic-resistant strains of bacteria and fungi. Iontophoretic silver treatment is somewhat more effective than treatment with silver compounds, with generally the same spectrum of activity as that of silver nylon. The effects of electrically-generated silver ions are described in a number of publications, including the following: J. A. Spadaro, et al., "Antibacterial Effects of Silver Electrodes with Weak Direct Current," Antimicrobial Agents & Chemotherapy, Vol. 6, pp. 637-642 (1974); T. J. Berger, et al., "Antifungal Properties of Electrically Generated Metallic Ions," Antimicrobial Agents & Chemotherapy, Vol. 10, pp. 856-860 (1976); R. O. Becker, et al., "Treatment of Orthopedic Infections With Electrically-Generated Silver Ions," J. Bone & Joint Surgery, Vol. 60-A, pp. 871-881 (1978)), incorporated herein by reference.

Silver and other metals are used in a number of wound dressings, in the form of pure metal, metal salts, or other compounds. Wound dressings that contain silver or silver compounds are described by McKnight, et al. (U.S. No. 3,800,792), Weaver, et al. (U.S. No. 5,218,973), Fabo (U.S. No. 5,340,363), Klippel, et al. (U.S. No. 3,830,908), Stowasser (U.S. No. 2,934,066), and Matson (U.S. No. 4,728,323). Dressings and devices for the administration of electrical stimulation include those described by Konikoff (U.S. No. 4,142,521), Rogozinski (U.S. No. 5,395,398), Silver, et al. (U.S. No. 4,703,108), D'Alerta (U.S. Patent No. 5,423,874), Jones (U.S. Patent No. 4,911,688), Juhasz (U.S. Patent No. 4,817,594), Seiderman (U.S. Patent No. 4,767,401), and Becker, et al. (U.S. No. 5,814,094, incorporated herein by reference). Antimicrobial dressings are described in our application Serial No. 09/431,991, filed 11/03/99 ("Multilayer Antimicrobial Treatment Device"), incorporated herein by reference.

Antimicrobial metal coatings may be formed by creating atomic disorder (i.e., high concentrations of point defects in a crystal lattice, vacancies, line defects) by vapor deposition under conditions which limit diffusion (Burrell, et al., U.S. No. 6,017,553, No. 5,958,440, and No. 5,454,886). Silver materials that form complex ions such as $Ag(CN)_2^-$, AgCN(aq)(ion pair), $Ag(NH_3)_2^+$, $AgCl_2^-$, $Ag(OH)_2^-$, $Ag_2(OH)_3^-$, $Ag_3(OH)_4^-$, and $Ag(S_2O_3)_2^{3-}$ also exhibit antimicrobial effects. The materials may be prepared as coatings, foils, powders, or fine grain or nanocrystalline powders formed with atomic disorder (U.S. No. 5,985,308).

Despite the availability of a variety of wound dressings, antimicrobial compositions, delivery systems (both passive and iontophoretic) for supplying bactericidal metals such as silver to a wound, and numerous deodorant and antiperspirant compositions, there is a continuing need for a simple, versatile, cost-effective material that is capable of supplying useful amounts of silver in a variety of applications.

DISCLOSURE OF THE INVENTION

According to its major aspects and broadly stated, the present invention includes a multilayered antimicrobial composition in sheet form, articles of manufacture that include the composition, and a method for making the composition. The composition includes a layer of silver (or other metal with useful antimicrobial properties) and a layer of polymer material; the silver layer may be provided by coating the polymer layer with silver, incorporating silver into the polymer layer, or attaching a silver-containing fabric to the polymer layer. The composition may be used in a variety of products, including but not limited to wound dressings, hot and cold packs, pressure dressings, knee, wrist and elbow sleeves, heel and sole inserts, socks, cushioning devices for use with orthotics, leg, thigh and body wraps, and the like.

The polymer material is an important feature of the present invention, and may be any of a variety of such materials that are at least somewhat flexible and conformable, and that can be shaped into substantially flat sheets or other useful configurations. Polymer materials that are somewhat resilient (i.e., compressible or "springy") are also broadly useful for providing a measure of shock-absorbing or shock-dampening capability to wound dressings, socks, orthotic inserts, wraps, and other articles made with the composition. For example, polymeric gel compositions that include a gel or combination of gels, foamed or non-foamed, with a durometer hardness that somewhat approximates that of human skin, are broadly suitable for the practice of the invention. Other suitable materials include block copolymers with, optionally, mineral oil, thermoplastic materials, and indeed any natural or synthetic materials with the requisite properties. Stretchable polymer materials are useful for pressure dressings, support wraps, and so forth.

Another important feature of the present invention is the silver layer. Silver is effective against a broad spectrum of microorganisms, including but not limited to sepsis-causing bacteria and odor-causing bacteria. The silver is preferably in a mechanically stable form that remains bound to the composition when dry, but that rapidly begins to release useful amounts of silver ions on a sustainable basis when moistened by a liquid such as water, saline solution, wound exudate, perspiration, and so forth. Thus, when the composition contacts the target area, at least a portion of the silver contained therein is released into the surrounding tissues with resulting beneficial effects.

The silver content of this layer is sufficient that, while wetted, the rate of release of silver ions quickly reaches a reproducible equilibrium level that remains approximately constant for an extended period of time. Thus, the composition can be used to treat a targeted area, removed at intervals, cleaned, re-wetted and reused. For treatment purposes, the useful lifetime of the composition depends on factors such as the silver content, the size and thickness of the composition, and the particular application.

In a preferred embodiment of the invention, the amount of silver released by the composition, and the rate of release of the silver, are sufficiently high to achieve beneficial effects yet low enough to avoid the deleterious effects (cytotoxicity, staining, tattooing) associated with long-term use of products that contain high concentrations of silver. The composition itself is durable, nontoxic, nonhazardous, substantially nonallergenic and nonirritating, and inert until activated by contact with a suitable liquid (water, perspiration, wound exudate, hydrocolloid, etc.). While silver is preferred, other metals, alloys, or compounds of these metals or alloys may also be useful.

When used in the care and treatment of skin infections, ulcers, surface wounds (including surgical incisions) and the like, the composition (and articles made therewith) is effective in slowing the growth of microorganisms such as bacteria and fungi in the treated area. The composition also provides an effective prophylactic measure against airborne contaminants and opportunistic infections.

Still another feature of the present invention is its versatility. The composition can be used in stand-alone form or to manufacture a variety of treatment devices. It may include layers of additional useful materials, including but not limited to moisture-impermeable layers, moisture-absorbing layers, inserts for providing heat or cooling, and additional layers of the polymer composition or the silver-containing layer. The composition is used in wound dressings, socks, stump socks, shoes, garment shields, knee, elbow and wrist sleeves, wraps, and a broad range of other articles of manufacture. The composition can be made by any convenient techniques known in the art, of readily available materials. It can be provided in a convenient form for a variety of applications, ranging from prepackaged, presterilized individual units such as Band-Aid® type dressings to rolls or sheets that can be cut to size as needed.

Other features and advantages of the present invention will be apparent to those skilled in the art from a careful reading of the Best Modes for Carrying Out the Invention presented below and accompanied by the drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings,

Fig. 1A–1C are cross-sectional views of multilayer compositions according to a preferred embodiment of the present invention;

Figs. 2A and 2B are plan views of additional multilayer compositions according to the invention;

Figs. 3A and 3B are perspective views of articles made with the composition;

Figs. 4A–4C show additional multilayer compositions according to the invention;

Figs. 5A and 5B are plan views of additional multilayer compositions according to the invention;

Fig. 6 is a cross-sectional view of another multilayer composition according to the invention;

Fig 7A is a graph of silver released per minute from a piece of a silver-containing fabric usable with the invention; and

Fig. 7B shows the total silver released over time for two test series of the fabric of Fig. 7A.

BEST MODES FOR CARRYING OUT THE INVENTION

In the following description of best modes for carrying out the invention, reference numerals are used to identify structural elements, portions of elements, surfaces or areas in the drawings, as such elements, portions, surfaces or areas may be further described or explained by the entire written specification. For consistency, whenever the same numeral is used in different drawings, it indicates the same element, portion, surface or area as when

first used. Unless otherwise indicated, the drawings are intended to be read together with the specification, and are to be considered a portion of the entire written description of this invention as required by 35 U.S.C. § 112.

In a preferred embodiment, the present invention is a multilayer composition 10 in sheet form, including a layer 12 of polymer material and a silver-containing layer 14 (shown schematically in Fig. 1A). Layer 12 may comprise a polymeric gel composition, for example, a block copolymer and, optionally, mineral oil as described below. As used herein, the term "block copolymer" refers to polymer compositions that contain long stretches of two or more monomeric units linked together by chemical valences in one single chain, including but not limited to styrene/butadiene, styrene-isoprene/butadiene, styrene-ethylene/butadiene and so forth. The silver layer 14 may be added by coating the polymeric gel composition with silver or incorporating silver therein; alternatively, a silver-containing fabric 16 such as silver nylon material may be attached to the polymeric gel composition (Fig. 1B). While silver is preferred, other metals and compounds with useful antimicrobial properties may also be useful.

Layer 12 preferably includes a polymeric material with an elongation of at least approximately 2%, more preferably, at least approximately 5%; however, materials with larger elongations (up to 2500% or even more) may also be useful. Layer 12 may be of any convenient thickness, for example, the layer may be (about 0.2–1.5 cm) thick, with a durometer hardness in the range of 0–20.

The polymeric gel composition of layer 12 preferably comprises a gel or combination of gels that are nonfoamed or foamed with, e.g., a foaming agent. The mineral oil may be present in from 0–95% by weight based on total gel weight, more preferably 70–90% by weight, but also including all of any positive amount including 5, 10, 15, 20, 25, 30, 35, 40, 45, 55, 60, 65, 70, 75, 80, 85, and 90% by weight and all values and ranges in between all these listed values. The gel preferably has a durometer (Shore A) of approximately 0–20 and preferably a durometer that matches or approximates (within about +20%) that of human skin. Preferably, the oil is present on an equal weight basis, or in a weight ratio of 1/4, with regard to the amount of polymeric material present. More preferably, the gel durometer is from 1–100 Shore 00, most preferably 5–35. The polymeric material present is preferably a styrene isoprene/butadiene block copolymer, a styrene-ethylene/butadiene-styrene, or a styrene-ethylene/propylene block copolymer. Examples of suitable polymeric materials include C-Flex 1970-W5 (R70-339-000), C-Flex 1960-W5 (both manufactured by Consolidated Polymer Technologies, Largo, Florida, U.S.A.), Kraton G1654 (manufactured by Shell Chemical Co.), Septon 4033, 4044, 4055, 4077, and 4099 (manufactured by Kuraray), DYNAFLEX G6703, G6708, G6713 and G2706 (manufactured by GLS Corp.). For the C-Flex materials a particularly preferred ratio is 1 part oil per 2 parts C-Flex material.

Preferred ratios of polymer to mineral oil are about 1/1–4/1 using C-Flex 1970-W5 or 1960-W5, one part Kraton G1654: 2.75 parts mineral oil, and 14 parts Kraton G1654: 15

parts C-Flex R70-306 (or R70-190 or R70-251 or any mixture thereof): 40 parts mineral oil. The C-Flex R70-339-000, R70-306, -190 and -251 materials are also preferred herein and are products of Consolidated Polymer Technologies. They are blends of S-EB-S block copolymer or SIB block copolymer with mineral oil. 10 parts Kraton G1654 and 11 parts C-Flex R70-306 and 27 parts Duoprime 70 oil is also preferred. A highly preferred gel is 62.5% C-Flex 1970-W5, and 37.5% Carnation mineral oil. 55-65% C-Flex 1970-W5 and 45-35% oil is also preferred. Also preferred is a composition of 26–65 wt% styrene-isoprene/ butediene block copolymer and 35–74% by weight mineral oil. Here, 27, 28, 29, 30, 35, 40, 45, 50 and 55 wt% SIB can be used with oil ranging from 73, 72, 71, 70, 65, 60, 55, 50 and 45 wt%. All %'s are percent by weight unless otherwise indicated.

The preferred polymers useful herein and listed above (C-Flex, Kraton, Septon, and DNYAFLEX materials), in addition to being styrene-isoprene/butadiene or styrene-ethylene/butadiene-styrene block copolymers (mixed with mineral oil in the case of at least the C-Flex 1970-W5, R70-339-000, R70-306, -190 and -251 materials) also include styrene-butadiene-styrene and any thermoplastic elastomer having the Shore A and/or Shore 00 characteristics listed above and capable of being blended with mineral oil. Mixtures of all mentioned polymers may be used, for example, blends comprising a rubber having a lower durometer (for example, approximately 1–10 on the Shore "A" scale) and a rubber having a higher durometer (approximately 11–20). These types of blends are capable of being stretched by 100% or more before tearing, and are capable of providing a form fit dressing due to their inherent elasticity. The mineral oil used herein is preferably purified mineral oil and is preferably USP grade. Carnation mineral oil is preferred. The optimum ratios of polymer to oil are best determined by a modest degree of experimentation in view of the particular selection of these materials and the intended application.

While the above-described materials are useful for the practice of the invention, it will be understood that other oils and polymeric materials (including but not limited to polymers, block copolymers, thermoplastic materials and elastomeric materials) may also be suitable. For example, layer 12 may be made of a thermoplastic material that softens when exposed to heat and returns to its original condition when cooled to room temperature. Suitable materials include polyvinyl chloride, nylon, fluorocarbon compounds, polyethylene, polyurethane, polystyrene, polypropylene, neoprene, and various cellulosic and acrylic resins. Cured and partially-cured polymers, including but not limited to polyamides, polyesters, regenerated cellulose, cellulose acetate, and mixtures thereof are broadly suitable for use with the invention.

Foamed or nonfoamed thermoplastic elastomers or rubber only can also be used in layer 12, alone or in conjunction with the above-described polymeric material. For purposes of this detailed description, the term "thermoplastic elastomers" has its typical meaning; the foamed materials can exclude mineral oil. The inclusion of thermoplastic elastomers in the

polymeric material (the mixture optionally being foamed) is advantageous in making products made therewith readily customizable.

Layer 12 or layer 14, or both, may also include additional constituents such as antioxidants (Vitamins A, B, C, E, or any other antioxidants commonly used in polymers), emollients, humectants, and other skin conditioning agents (mineral oil, baby oil, aloe vera, beta glucan, etc.), anti-inflammatory agents, antimicrobial agents (as defined above) and other medicaments, and biocompatible preservatives, fragrances, and coloring agents. The constituents of layers 12, 14 are further selected to form stable compositions, that is, neither the constituents nor the compositions as a whole deteriorate or undergo cross-reactions during normal storage.

One or both sides of layer 12 are at least partially coated with silver by any convenient technique, including but not limited to vapor coating, aerosolized deposition, sputter coating, magnetron sputtering, vacuum evaporation, chemical deposition, plating, ion plating, or other techniques known in the art. Alternatively, the silver may be carried by a layer 16 that incorporates or is coated with useful amounts of silver. For example, layer 16 may comprise a woven, knitted, or nonwoven silver-plated fabric, or a fabric made up of a mat or mesh of fibers. Alternatively, the fabric may be made of a combination of silver-coated (or silver-impregnated) and plain fibers. Suitable materials for layer 16 include silver-impregnated warp knit nylon fabric, silver-impregnated nylon pile fabric, and other fabrics made by Omnishield, Inc., Swift, Inc., Sauquoit Industries, and other manufacturers. Other useful fabrics or textiles include those fabricated of natural fibers (cotton, silk, jute, linen, etc.), synthetic fibers (polyethylenes, rayons, acrylics, modacrylics, and others), and combinations thereof that contain useful amounts of silver.

Fabrics or textiles useful for the present invention may have any thickness, and preferably some degree of elasticity. That is, the fabrics are stretchable in at least one, preferably two, directions, with an elongation ranging from approximately 2% to 100% or more. For added stretchability, the fabric may include stretchable fibers (natural or synthetic rubber, LYCRA, etc.). The fabrics may be treated or finished in any manner known in the art. For example, a tricot, brushed, or pile surface may be applied to the surface of the fabric.

In one preferred embodiment of the present invention, layer 16 contains at least approximately 2 wt.% silver, more preferably at least approximately 5–20 wt.% silver. However, it should be noted that silver concentrations outside the preferred range may also be useful for some applications. Fabrics that are capable of providing beneficial amounts of silver in vivo, regardless of the silver content of the fabrics themselves, are broadly useful for the practice of the invention. Thus, the silver content of layer 16 (and, if present, layer 14) is sufficient that, when wetted with a suitable electrolyte, the rate of release of silver ions quickly reaches an equilibrium level that is sustainable for at least approximately 24 hours, preferably longer. Thus, composition 10 can be used to treat a targeted area for a selected period of time, removed, cleaned, re-wetted and reused. As will be evident, the useful

lifetime of composition 10 depends on factors such as the silver content, the size and thickness of the composition, and the particular application.

In a preferred embodiment, the amount of silver released by composition 10, and the rate of release of the silver, are high enough to produce beneficial effects but low enough to avoid deleterious effects such as cytotoxicity and staining that are sometimes associated with the use of products that contain high concentrations of silver.

Silver (or some other metal or compound with medically useful properties) is added to the fabric substrate of layer 16 by vapor coating, aerosolized deposition, sputter coating, chemical deposition, plating, or any other suitable technique. Individual fibers can be coated and then worked (woven, knitted, crocheted, felted, blown, etc.) into a fabric; alternatively, silver may be added to the finished fabric. Useful fabrics may contain up to 100% silver-containing fibers. The silver of layers 14, 18 is preferably in a highly purified form, that is, at least approximately 99.9% pure and preferably at least approximately 99.99% pure. The metal content of layers 14, 16 as well as the thickness, structure, and uniformity of the metal coating, may vary broadly depending on the intended application. However, it should be understood that the materials for layers 14, 18 are selected with a view to providing the needed amounts of free silver to the treatment site. Other metals that exhibit antibacterial and/or antifungal properties may also be useful for the practice of the present invention, including but not limited to gold, copper, platinum, aluminum, zinc, titanium, and combinations and alloys thereof.

Layers 14, 16 not only contain a sufficiently high content of silver (or other useful metal) to provide useful amounts of silver ions for the intended application, but preferably have an approximately uniform distribution of silver. Non-uniform distributions may result in non-uniform treatment, since the amount of silver supplied to different areas of the target site may differ. The thickness of the silver coating may vary broadly. Useful amounts of silver may be achieved with coatings no greater than 1 or 2 micrometers thick.

The silver in layers 14, 16 is preferably in a form that, when composition 10 is placed in contact with body tissues and moistened by a suitable liquid, releases silver ions by the passive dissolution of silver in an ionic form from the metallic silver surface in a process known as oligodynamic action. Thus, over a period of time, at least a portion of the available silver migrates to the immediately-adjacent tissues where it has useful antimicrobial and antifungal effects.

While not wishing to be bound by theory, it is believed that metallized (i.e., metal-containing, metal-coated, metal-plated) materials wherein the metal atoms are firmly attached or bound to a fabric substrate when dry, but are at least somewhat releasable in ionic form when wetted with a suitable liquid, are especially suitable for the practice of the present invention. For example, layers 14, 16 may contain silver in the form of small crystals which tend to release free silver ions when wetted by saline, water, wound exudate, or other suitable liquid. Crystalline silver deposits of this type, including microcrystalline and nanocrystalline

deposits, are believed to have a greater effective surface area than conventional silver-plated coatings, and therefore the capability of releasing more silver ions per unit coating weight, in shorter periods of time.

Other types of silver-containing materials may also be useful, where the silver (or other antimicrobial metal) is be in the form of a powder, flakes, foil, coating, or other useful form. For example, antimicrobial metals in powder form may be deposited onto a substrate, forming a coating with sufficient atomic disorder that the resulting material releases atoms, ions, molecules, or clusters containing silver on a sustained basis when in contact with an alcohol or a water based electrolyte (see, for example, U.S. No. 5,958,440 and U.S. No. 6,017,553). This type of coating, and other useful types of coatings, may be formed on layer 16, or directly on one or both surfaces of layer 12.

Layer 16 may be attached to polymeric gel composition layer 12 by any convenient means, including but not limited to heat/pressure bonding, crimping, embossing, sonic welding, needle punching and biocompatible adhesives. Alternatively, hook-and-loop or groove-and-rib type closures may be useful, particularly for applications where a removable layer 16 is desired. These types of closures are described in co-pending applications Serial Nos. 09/431,991, filed November 3, 1999, and 09/496,766, filed February 3, 2000, the disclosures of which are incorporated herein by reference.

Layer 16 is generally approximately 0.05–1.5 cm thick (although thicknesses outside this range may also be useful), and may be marked in some way so that the user can clearly distinguish the outer surface of layer 16 from the opposing outer surface of layer 12. For example, layers 12 and 16 may be of different colors, or one of the layers may carry tags or other surface features that help the user distinguish one of the layers from the other. Thinner layers 16 are suitable for dressings, wraps, and so forth. Thicker layers 16, including those made of compressible silver-containing fabric, are suitable for treating deeper wounds and other applications where a compressible layer 16 facilitates conforming the dressing to the region being treated.

Suitable fabrics for layer 16 include silver-impregnated brush tricot nylon, knit loop nylon, nylon pile fabric, and other fabrics that contain useful amounts of silver. Fabrics made of cotton, silk, rayon, polyester, dacron, acrylic and modacrylic, and other natural or synthetic materials, or combinations thereof, may also be useful. Suitable fabrics are made by Omnishield, Inc., Swift, Inc., Sauquoit Industries, and other manufacturers. As noted above, silver may be added to the fabric by any suitable technique, preferably a technique that produces a fabric wherein the filaments comprising the fabric are plated or coated with silver so that the silver is not just on the visible surface of the fabric. Indeed, the metal content of layer 16 as well as the thickness, structure, and uniformity of the metal coating, may vary broadly depending on the intended application. Fabrics with silver contents as low as 2 wt.% may be useful; however, those with higher silver contents (as high as 30 wt.%) are generally preferred. However, it should be understood that the material for layer 16 is selected with a

view to providing the needed amounts of free silver to the treatment site. Other metals that exhibit antibacterial and/or antifungal properties may also be useful for the practice of the present invention, including but not limited to gold, copper, platinum, aluminum, zinc, titanium, and combinations and alloys thereof.

Composition 10 may include additional layers. For example, composition 10 may have an outer layer of gas-permeable, moisture-impermeable material (GORETEX or the like), a layer of moisture-absorbing material interposed between layers 12 and 16, or a layer 18 of hook-and-loop fabric such as VELCRO between layers 12 and 16 (Fig. 1C). Alternatively, composition 10 may have a silver-containing layer such as layer 16 interposed between two layers 12, or comprise a layer 12 that itself contains silver.

Silver ions released by layers such as above-described layers 14 and 16 have been demonstrated to be effective against wound sepsis and odor-causing bacteria (including antibiotic-resistant strains, Gram-positive strains, and Gram-negative strains), as described in applications Serial Nos. 09/431,991 and 09/496,766, the disclosures of which are incorporated herein by reference.

The present invention is further illustrated by the following non-limiting examples.

EXAMPLE 1

The antimicrobial activity of composition 10 was tested on several bacterial strains obtained from the American Type Culture Collection ("ATTC"). Test materials included composition 10 (consisting of a polymeric gel layer 12 and a layer 16 of silver-containing nylon fabric) and a silver-containing nylon fabric alone. Eighteen-millimeter discs of each material were prepared and tested in vitro using a modified Kirby-Bauer protocol, wherein the discs were applied directly to newly-inoculated Kirby-Bauer plates, moistened with sterile saline solution, and incubated. Zones of inhibition were measured for each material after 48 hours of incubation. Results indicated that the antimicrobial activity of composition 10 was comparable to that of silver-containing nylon fabric.

EXAMPLE 2

Thirty-gram discs of silver-containing nylon fabric of a type usable for layer 16 were placed in (a) distilled, deionized water and (b) cell culture medium (Eagle's MEM), and maintained at room temperature (about 21–22° C). The silver content of the liquid media was assayed over a 48-hour period. In both water and culture medium, the maximum rate of silver release from the fabric discs was attained during the first 3 minutes of immersion; equilibrium was reached within a few hours. Thereafter, the rate of silver release was approximately constant for over 48 hours. Fig. 7A shows the rate of silver released per minute over a 35-minute period for a typical 30-gram disc immersed in water: the rate of

release quickly reached a maximum of 0.35 PPM, decreased to a plateau of approximately 0.04 PPM, and thereafter remained approximately constant. Fig. 7B shows the total amount of silver released over time, for two test series using discs of the same fabric. The output of silver ions was greater in culture medium than in water, due to the greater number of receptor molecules present in the culture medium.

EXAMPLE 3

Volunteer Patient A was a 59 year old retired well driller, male insulin-dependent diabetic, bilateral below-knee amputee with multiple problems including severe neuropathy and renal failure. Prior to treatment with the invention, Patient A developed a pressure ulcer measuring 2 cm in diameter on the end of his left stump. Bactroban, a prescribed antibiotic ointment, was applied when the ulcer was infected, and various dressings had been tried when drainage was heavy. The ulcer persisted for a period of 2–3 years.

All volunteer patients were advised of the experimental nature of the proposed treatment, and were assured that they could terminate the treatment at any time. Treatment with a silver-containing dressing according to the invention was initiated after obtaining the patient's informed consent.

A dressing consisting of an appropriately-sized sheet of composition 10 was applied, with silver-containing layer 14 engaging the ulcer; the dressing was changed daily. Within 10 days, the size of the ulcer was reduced by half without the development of a callus. Within 30 days, the ulcer was totally healed.

The patient developed a second pressure ulcer located at the back of his right stump, started by pressure contact with the edge of the prosthetic socket. The ulcer was approximately 12.7 cm wide by 7.6 cm long, and deep enough to expose muscle tissue.

Treatment with a dressing of composition 10 was started. Initially, the patient only changed the dressing every 3 days because of difficulties in accessing the ulcer site and of properly positioning the dressing on the ulcer. After one month, the site exhibited a strong odor, localized cellulitis, and heavy drainage. At that point, a bandage system was devised that allowed the patient to wrap a large piece of composition 10 in place over the ulcer and to secure it with VELCRO fasteners. The patient responded well to the ease of use and began changing the dressing daily.

After an additional 30 days of treatment the ulcer had reduced to about 3 cm wide by 1 cm long. The wound was totally granulated and the depth was superficial. The resulting scar is excellent and not prone to breakdown. A new prosthetic socket was devised to prevent recurrence.

EXAMPLE 4

Patient B was a 64 year old female retired registered nurse, insulin-dependent diabetic, with a partial amputation of the right foot. The amputation level was poorly placed, resulting in shearing gait and development of a chronic ulcer on the posterior sole approximately 3.5 cm in diameter. Antibiotic therapy was unsuccessful.

A dressing of composition 10 was applied to the ulcer; the patient was fitted with a padded walking cast, with gait correction. The cast was removed one week later. At that time, the ulcer was clean with initial healing of about 30% of the wound area. A second dressing (also of composition 10) and cast were applied. The second cast was removed at the end of the second week, at which time the wound had reduced to 0.8 cm in diameter. The wound was dressed and cast in the same fashion for a third week of treatment, at which time the wound was completely healed and the patient provided with an appropriate prosthesis. The treating surgeon indicated that healing time had been reduced to 50% of what he expected, based on a prior episode with this patient.

Composition 10 may be provided in virtually any size, thickness, and configuration, including both flat and shaped sheets. The composition may be used for wraps and wound dressings (including pressure dressings). It may also be used to manufacture articles such as knee, elbow, and wrist sleeves, antibacterial inserts and dressings such as those described in the above-referenced patent applications, cushioned socks, sleeves, and the like worn to minimize the discomfort of orthotic and prosthetic devices, and articles for the provision of heat/cooling to a treatment site. Composition 10 may be shaped into articles such as heel orthoses, sole pads, garment shields, and other items used to increase user comfort, or interposed between the skin and conventional hot or cold packs for added comfort and safety. Polymeric layer 12 may be a material that is at least somewhat compressible or resilient (i.e., "springy"), to provide a degree of shock-absorbing or shock-dampening for wound dressings, socks, stump socks, and so forth. Silver-containing layer 16 may also be compressible (as noted above, a composition 10 with a compressible layer 16 may be used for packing deep wounds where a conformable packing material is desired). Composition 10 in any of its preferred embodiments may also be used in the applications described in U.S. Patents Nos. 5,603,122 and 5,830,237, both incorporated herein by reference.

Composition 10 may be used in applications requiring hot or cold packs. When heated or cooled, the gel composition of layer 12 retains its temperature and slowly returns to ambient temperature, thus, composition 10 can provide heating or cooling in a manner similar to that of a convention hot or cold dressing. If desired, a sheet 20 of composition 10 may include one or more pockets 22 for holding removable heated or cooled inserts 24 as shown in Fig. 2A. Alternatively, sheet 30 may have a plurality of permanent inserts 32 (Fig. 2B). Inserts 24 and 32 are preferably made of a material with a high heat capacity, thus, the inserts tend to retain their temperature when heated or cooled and only slowly return to ambient temperature. If preferred, inserts 24 may be replaced by suitable amounts of crushed ice.

Wound dressings that include a layer of composition 10 are shown in Figs. 3A and 3B. A multilayer dressing 40 has a thin, flexible outer layer 42 and a layer 44 of composition 10 (for clarity, silver-containing layer 16 is shown partially peeled away) (Fig. 3A). Layer 42 may be made of a thermoplastic material that softens when exposed to heat and returns to its original condition when cooled to room temperature. Suitable materials include polyvinyl chloride, nylon, fluorocarbon compounds, polyethylene, polyurethane, polystyrene, polypropylene, and various cellulosic and acrylic resins. Alternatively, layer 42 may be made of GORETEX or other suitable material.

Layer 44 has a plurality of throughholes 46 arranged in any convenient pattern. A sponge 48 is inserted in each throughhole 46, so that sponges 48 contact silver-containing layer 16. Sponges 48 are made of a soft, flexible and conformable, moisture-absorbing material, including but not limited to cotton, polyester, rayon, dacron, polyurethane, polypropylene, acrylics and modacrylics, polyvinyl acetate or other synthetic materials, or combinations thereof, in woven, nonwoven, foam, or sponge-like form. Layer 44 and sponges 48 need be no more than a few millimeters thick for most applications. Sponges 48 are wetted to provide a moisture reservoir for silver-containing layer 16 when dressing 40 is in use.

The edges of layers 42 and 44 may be attached together by any convenient technique, including but not limited to application of heat and pressure, embossing, crimping, sonic welding, needle punching, and biocompatible adhesives. However, techniques which avoid the use of adhesives, fixatives, and so forth are preferred.

Another dressing 50 has a layer of composition 10 (with moisture-absorbing sponge inserts 48). A groove 52 is formed near a perimeter 54 of composition 10, and a corresponding rib 56 near a perimeter 58 of outer sheet 42. Groove 52 and rib 56 form a fastener that allows the user to wholly or partly remove outer sheet 42 from dressing 50, for example, to add additional water to sponges 48 so as to maintain an effective moisture reservoir for the silver-containing layer of composition 10. Outer sheet 42 can easily be replaced simply by pushing rib 56 back into groove 52.

Additional embodiments of the present invention are shown in Figs. 4A–4C. By way of example, composition 10 may include a layer 60 of moisture-absorbing material interposed between layers 12 and 16 (or 14), as shown in Fig. 4A.

To provide for ventilation of wounds, composition 10 may have a plurality of throughholes 62 (Fig. 4B), a series of ridges or other suitable structures formed in the wound-contacting surface (for example, ridges 64 shown in Fig. 4C). Throughholes 62 may be approximately 1 mm in diameter or thereabouts, spaced approximately 5 mm apart; ridges 64 are at least approximately 1 mm high. The provision of throughholes 62 and/or ridges 64 allows for a degree of air circulation for ventilation purposes, which is particularly useful for larger-area wounds treated with composition 10 or articles made therewith.

When used as a dressing, a sheet of composition 10 may be retained in position by a separate bandage, clip, safety pin, or other fastener. For example, metal clips and other fasteners such as those used with the familiar ACE bandages may be useful. Hook-and-loop closures may be attached directly to composition 10 (if desired, composition 10 may have a fabric layer that facilitates attachment of such closures).

A length of composition 10 with a hook-and-loop closure (VELCRO or the like) is shown in Fig. 5A. A piece 70 of loop-type fabric is attached at one end of composition 10, and a mating piece 72 of hook-type fabric is attached at the other end (preferably, piece 70 is attached to layer 12, and piece 72 to silver-containing layer 16). Alternatively, pieces 70 and 72 may be replaced by the mating portions of a snap, buckle, clasp, or other fastener. In use, composition 10 is wrapped around a limb or other body part and pieces 70, 72 mate and help secure the wrap or dressing so formed in position.

Another embodiment of composition 10, shown in Fig. 5B, has one or more strips of fabric 74 at intervals. Fabric 74 is any type of woven, nonwoven, or knitted fabric (or indeed any other type of material) that is capable of supporting a closure such as a bandage clip, safety pin, snap, clasp, or other fastener.

Still another embodiment of composition 10 is shown in Fig. 6, wherein a fabric layer 80 is attached to polymer 12 on the opposite face from silver-containing layer 16 (as will be evident, a fabric layer 80 may also be used with the embodiments shown in Figs. 1A and 1C). Layer 80, which need not contain silver or other bactericidal metal, is positioned on the outside when composition 10 is used in a wound dressing (that is, silver-containing layers 14 or 16 contact the treatment area). Thus, a clip, safety pin, or other closure may be secured to layer 80 to secure the dressing formed by composition 10 in position.

Composition 10 (and articles made with the composition) can be manufactured in a variety of useful shapes for use in different applications or on different wound sites. A sheet of composition 10 could, for example, include one or more slits or throughholes for accommodating a drain, catheter, external fixation device, or the like.

Composition 10 is inert until the silver of layer 16 (or 14) is wetted by any of a variety of agents: water, wound exudate, or other suitable liquid. Then, at least some free silver ions are released from layers 14 or 16 and migrate from composition 10 into the surrounding region. When placed so that layer 14 or 16 contacts the wound surface, naturally-occurring body fluids may be sufficient to activate this process. More frequently, composition 10 is activated by moistening with a suitable liquid to promote the release of free ions. Distilled or sterile water is preferred, since tap water tends to vary in quality and frequently contains ions which interfere with the emission of silver from layers 14 or 16. Hydrocolloid preparations such as DuoDerm™ (manufactured by Convatec) may be useful in maintaining moisture in composition 10 and articles made therewith, and do not interfere with silver ion emission.

Composition 10 (and articles made therewith) is self-sterilizing, that is, layers 14 and 16 sterilize themselves when wetted as a result of the antimicrobial effect of the silver

contained in these layers. As a result, even though a composition 10 need be used only once, it may be kept in position for extended periods of time, or be rinsed and reused.

An antimicrobial composition according to the present invention provides prophylactic and/or therapeutic activity to help prevent (or treat) infection, provide anti-inflammatory and anti-allogenic effects, and promote healing. Importantly, while the device has significant bactericidal, anti-inflammatory, and anti-allogenic effects in the treated area, these effects are achieved without concurrent cell damage. The optimum content of silver (or other useful metal or compound) depends on the particular application; thus, compositions with silver contents outside the above-quoted ranges may also be useful for the practice of the invention.

Composition 10 is flexible and conformable to the area to be treated. In one preferred embodiment, the composition is also at least somewhat resilient and shock-absorbing; in another preferred embodiment, one or more of its layers are at least somewhat compressible. The optimum dimensions and configurations of the composition, and articles made with the composition, depend on the size and location of the area to be treated, and include considerations of affixing the device in place, controlling moisture loss, and ensuring direct contact between silver-containing layers 14 or 16 and the area to be treated. Layers 14, 16 are not known to cause allergic reactions, thus, their use prevents some of the potentially-harmful side effects associated with other silver delivery systems (such as topical preparations containing silver sulfadiazine, silver thiosulfate, and other silver compounds). Composition 10 is nonhazardous, conformable to the shape of the site to be treated, readily adaptable to diverse clinical situations, and safe and easy to use. Furthermore, the composition provides a sustainable, beneficial amount of silver to the treated area while avoiding dosages that may lead to deleterious effects.

With respect to the above description of the invention, it is to be realized that the optimum dimensional relationships for the parts of the invention, to include variations in size, materials, shape, form, function and manner of operation, assembly and use, are deemed readily apparent and obvious to one skilled in the art, and all equivalent relationships to those illustrated in the drawings and described in the specification are intended to be encompassed by the present invention.

Therefore, the foregoing description is considered as illustrative only of the principles of the invention. Further, since numerous modifications and changes will readily occur to those skilled in the art, it is not desired to limit the invention to the exact construction and operation shown and described, and accordingly, all suitable modifications and equivalents may be resorted to, falling within the scope of the invention. Thus, it will be apparent to those skilled in the art that many changes and substitutions can be made to the preferred embodiment herein described without departing from the spirit and scope of the present invention as defined by the appended claims.

WHAT IS CLAIMED IS:

1. A multilayer composition, comprising:

a first layer of polymeric material; and

a second layer engaging at least one side of said first layer, said second layer containing a bactericidal metal.

2. The composition as recited in claim 1, wherein said first layer further comprises a gel composition including a block copolymer and mineral oil.

3. The composition as recited in claim 1, wherein at least a portion of said bactericidal metal is silver.

4. The composition as recited in claim 1, wherein at least a portion of said bactericidal metal is crystalline silver.

5. The composition as recited in claim 1, wherein said second layer is selected from the group consisting of (a) a coating on said first layer, said coating containing said bactericidal metal, (b) a quantity of said bactericidal metal in said first layer, and (b) a silver-containing material attached to said first layer.

6. The composition as recited in claim 1, wherein said second layer further comprises silver-containing nylon fabric.

7. The composition as recited in claim 1, wherein said second layer further comprises silver-containing nylon fabric containing fibers, wherein at least a portion of said fibers in are coated with silver.

8. The composition as recited in claim 1, wherein said bactericidal metal further comprises silver, said silver mechanically attached to said second layer so that, when said second layer is wetted, at least a portion of said silver is released in the form of ionic silver.

9. The composition as recited in claim 1, wherein said bactericidal metal further comprises silver, said second layer releasing silver ions at a sustainable rate when said second layer is wetted.

10. The composition as recited in claim 1, further comprising at least one third layer, said at least one third layer made of moisture-absorbing material, moisture-permeable material, moisture-impermeable material, or gas-permeable material.

11. The composition as recited in claim 1, wherein at least one of said first and second layers is at least somewhat resilient.

12. The composition as recited in claim 1, wherein at least one of said first and second layers is at least somewhat flexible and conformable.

13. The composition as recited in claim 1, wherein at least one of said first and second layers is at least somewhat compressible.

14. The composition as recited in claim 1, wherein said composition has an elongation of at least approximately 2%.

15. The composition as recited in claim 1, wherein at least one of said first and second layers further comprises a constituent selected from the group consisting of antioxidants, emollients, humectants, skin conditioning agents, anti-inflammatory agents, antimicrobial agents, medicaments, preservatives, fragrances, coloring agents, thermal-regulating agents, and mixtures thereof.

16. The composition as recited in claim 1, further comprising closure-facilitating means operably connected to said composition.

17. An article of manufacture, said article comprising:

a multilayer composition including

a first layer of polymeric material, and

a second layer engaging at least one side of said first layer, said second layer containing a bactericidal metal.

18. The article as recited in claim 17, wherein said first layer further comprises a polymeric gel composition including a block copolymer and mineral oil.

19. The article as recited in claim 17, wherein at least a portion of said bactericidal metal is silver.

20. The article as recited in claim 17, wherein at least a portion of said bactericidal metal is crystalline silver.

21. The article as recited in claim 17, wherein said second layer is selected from the group consisting of (a) a coating on said first layer, said coating containing said bactericidal

metal, (b) a silver-containing material attached to said first layer, and (c) a quantity of said bactericidal metal in said first layer.

22. The article as recited in claim 17, wherein said composition further comprises a layer of moisture-absorbing material, moisture-permeable material, moisture-impermeable material, or gas-permeable material.

23. The article as recited in claim 17, wherein said second layer further comprises silver-containing nylon fabric.

24. The article as recited in claim 17, wherein said second layer further comprises silver-containing nylon fabric containing fibers, wherein at least a portion of said fibers are coated with silver.

25. The article as recited in claim 17, wherein at least one of said first and second layers is at least somewhat flexible and conformable.

26. The article as recited in claim 17, wherein at least one of said first and second layers is at least somewhat resilient.

27. The article as recited in claim 17, wherein said composition has an elongation of at least approximately 2%.

28. The article as recited in claim 17, wherein at least one of said first and second layers further comprises a constituent selected from the group consisting of antioxidants, emollients, humectants, skin conditioning agents, anti-inflammatory agents, antimicrobial agents, medicaments, preservatives, fragrances, coloring agents, thermal-regulating agents, and mixtures thereof.

29. The article as recited in claim 17, wherein said bactericidal metal further comprises silver, said second layer releasing silver ions at a sustainable rate when said second layer is wetted.

30. The article as recited in claim 17, wherein said bactericidal metal further comprises silver, said silver mechanically attached to said second layer so that, when said second layer is wetted, at least a portion of said silver is released in the form of ionic silver.

31. The article as recited in claim 17, wherein at least one of said first and second layers is at least somewhat compressible.

32. A method for making a multilayer composition in sheet form, said method comprising the step of attaching a first layer of polymeric material to a second layer, said second layer containing a bactericidal metal.

33. The method as recited in claim 32, wherein said first layer further comprises a gel composition including a block copolymer and mineral oil.

34. The method as recited in claim 32, wherein at least a portion of said bactericidal metal is silver.

35. The method as recited in claim 32, wherein at least a portion of said bactericidal metal is crystalline silver.

36. The method as recited in claim 32, wherein said second layer is selected from the group consisting of (a) a coating on said first layer, said coating containing said bactericidal metal, (b) a quantity of said bactericidal metal in said first layer, and (c)a silver-containing material attached to said first layer.

37. The method as recited in claim 32, wherein said second layer further comprises silver-containing nylon fabric.

38. The method as recited in claim 32, further comprising the step of attaching at least one third layer to said composition, said at least one third layer made of moisture-absorbing material, moisture-permeable material, moisture-impermeable material, or gas-permeable material.

39. The method as recited in claim 32, further comprising the step of selecting at least one of said first and second layers from the group of at least somewhat flexible and conformable materials.

40. The method as recited in claim 32, further comprising the step of selecting at least one of said first and second layers from the group of at least somewhat compressible materials.

41. The method as recited in claim 32, further comprising the step of selecting at least one of said first and second layers from the group of at least somewhat resilient materials.

42. The method as recited in claim 32, wherein at least one of said first and second layers has an elongation of at least approximately 2%.

43. The method as recited in claim 32, further comprising adding to at least one of said first and second layers a constituent selected from the group consisting of antioxidants, emollients, humectants, skin conditioning agents, anti-inflammatory agents, antimicrobial agents, medicaments, preservatives, fragrances, coloring agents, thermal-regulating agents, and mixtures thereof.

44. The method as recited in claim 32, wherein said bactericidal metal further comprises silver, said silver attached to said second layer so that, when said second layer is wetted, at least a portion of said silver is released in the form of ionic silver.

45. The method as recited in claim 32, wherein said second layer further comprises silver-containing nylon fabric containing fibers, wherein at least a portion of said fibers are coated with silver.

46. The method as recited in claim 32, further comprising the step of selecting said second layer from the group of silver-containing fabrics that are capable of releasing silver ions at a sustainable rate when wetted.

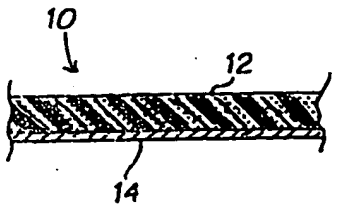


Fig. 1A

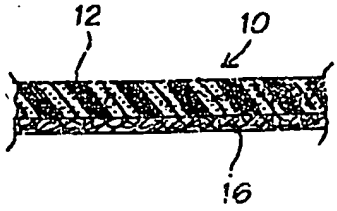


Fig. 1B

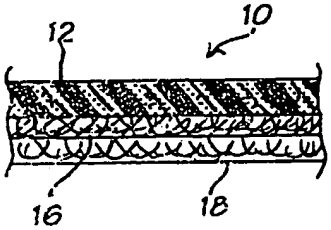


Fig. 1C

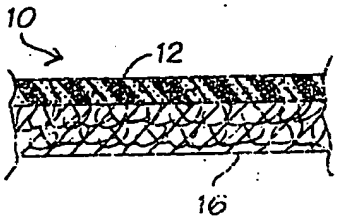


Fig. 1D

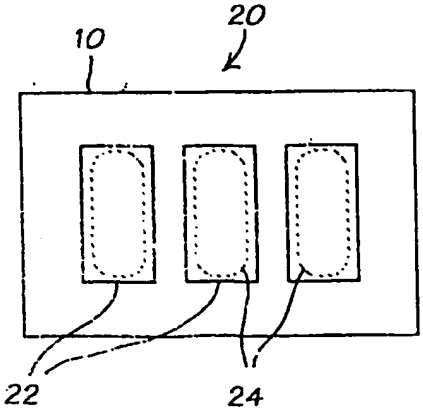


Fig. 2A

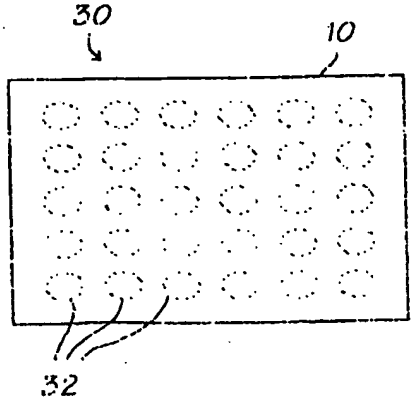


Fig. 2B

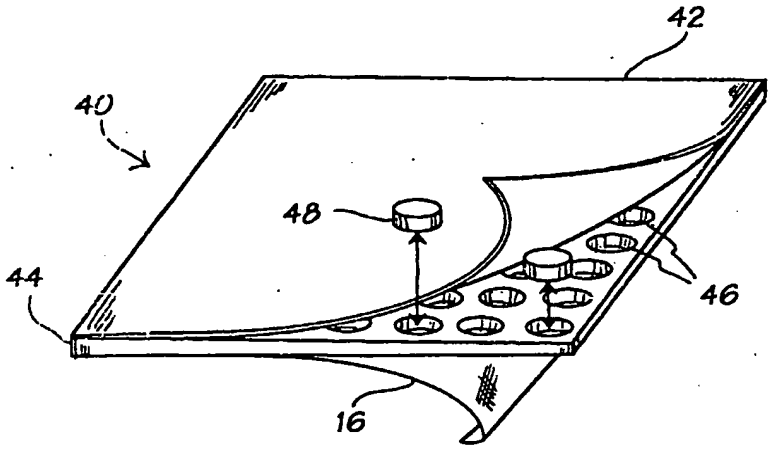


Fig. 3A

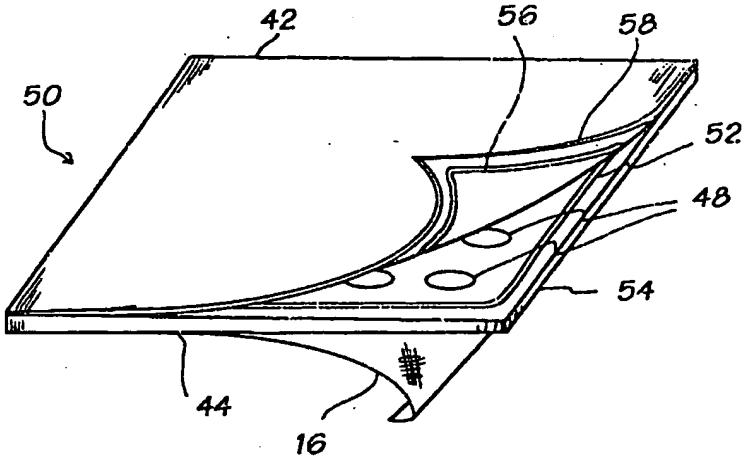


Fig. 3B

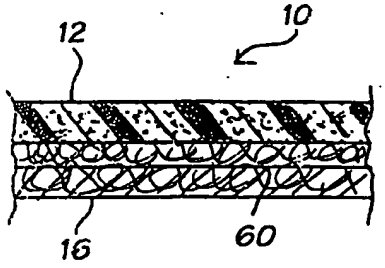


Fig. 4A

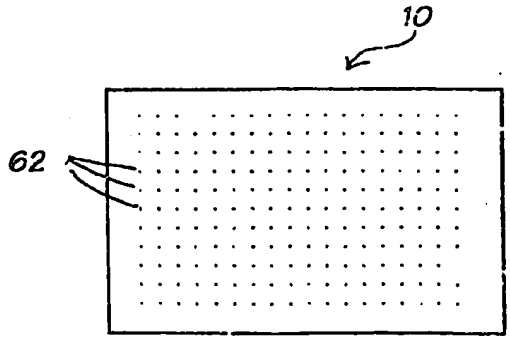
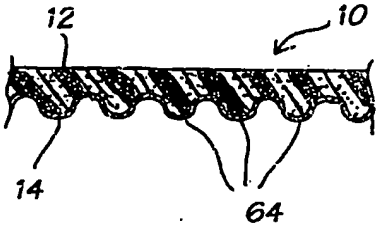


Fig. 4B

Fig. 4C



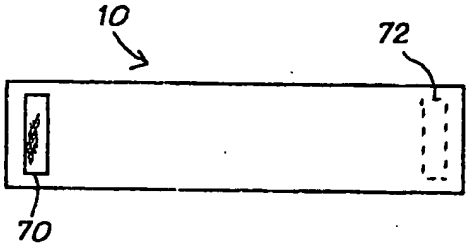
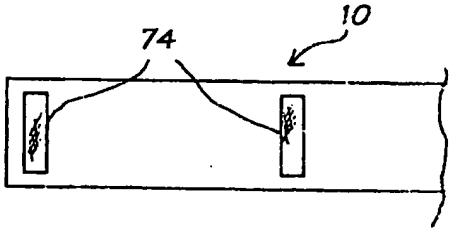


Fig. 5A

Fig. 5B



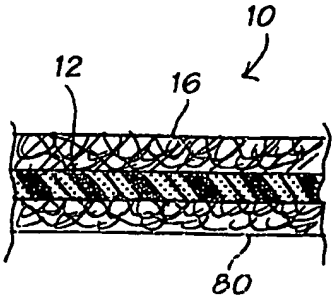


Fig. 6

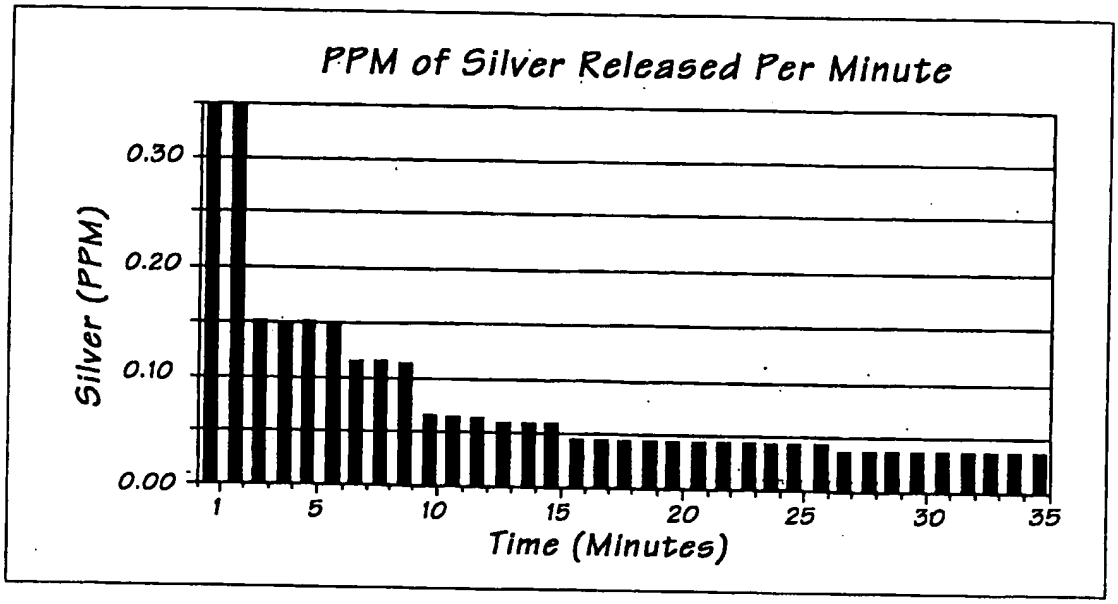

PPM of Silver Released Per Minute
Silver (PPM)
0.30
0.20
0.10
0.00
1
5
10
15
20
25
30
35
Time (Minutes)

Fig. 7A

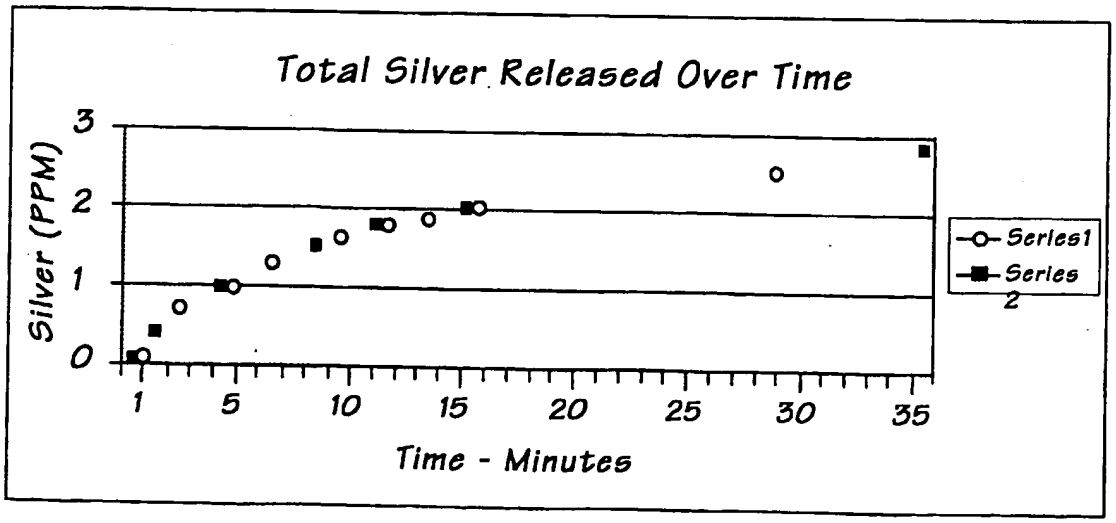

Total Silver Released Over Time
Silver (PPM)
3
2
1
0
1
5
10
15
20
25
30
35
Time - Minutes
Series1
Series 2

Fig. 7B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/04882

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :Please See Extra Sheet.
US CL :Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

PALM

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	US 6,087,549 A (FLICK) 11 July 2000, see entire document.	1-46
A	US 4,959,268 A (HAGIWARA et al.) 25 September 1990, see entire document.	1-46
A,P	US 6,040,251 A (CALDWELL) 21 March 2000, see entire document.	1-46
Y	JP 4-275142 A (CHISSO CORPORATION)30 September 1992, see abstract provided.	1-46

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
20 MARCH 2001	08 MAY 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MS. ARTI SINGH Telephone No. (703) 308-0661

Form PCT/ISA/210 (second sheet) (July 1998) *